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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/683,583	10/09/2003	Larry Bock	40-001210US	7722

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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

EXAMINER	
LUNDGREN, JEFFREY S	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 07/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/683,583	BOCK ET AL.	
	Examiner	Art Unit	
	Jeff Lundgren	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-81* is/are pending in the application.

4a) Of the above claim(s) *3-6,10-15 and 17-81* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7 and 16* is/are rejected.

7)☒ Claim(s) *8 and 9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *see office action*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election of Invention and Status of the Claims

Applicant's election with traverse of Group I, claims 1-9 and 16, in the reply filed on April 3, 2005, is acknowledged. The traversal is on the grounds that the art require for the search and examination of multiple groups in not largely divergent and do not create a serious burden to search all inventions, and are not anticipated by the art of record.

As communicated in the Restriction Requirement, the art is divergent, and a reference which anticipates one invention, Group II, does not necessarily anticipate another invention (i.e., claim 1 of Group I), and therefore would create a serious burden upon the Office to search and examine more than a single invention. For example, consider the teaching of Cui et al., in the rejection of claim 1 under 35 U.S.C. § 102(b) as detailed below.

Regarding Applicants' comments toward Chao and Lee, this is not found persuasive because each of Chao and Lee are capable of alternatively using the inventions of Groups II and IV as indicated. For example, see Fig 3a and 3b in Chao, and description thereof regarding functionalized Pt nanonwire.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-81 are pending in the application; claims 10-15 and 17-81 are withdrawn as being directed to a non-elected invention; claims 3-6 are withdrawn as being drawn to a non-elected species until a generic claim from which they depend is found allowable; claims 1, 2, 7-9 and 16 are the subject of the Office Action below.

Information Disclosure Statement

The information disclosure statements (IDSs) submitted on March 10, 2004, and January 21, 2005, have been considered by the Examiner. The submission is in compliance with the provisions of 37 CFR § 1.97. Enclosed with this Office Action is a return-copy of the Form PTO-1449 with the Examiner's initials and signature indicating those references that have been considered.

Objection to the Abstract Under 37 C.F.R. § 1.72

The abstract of the disclosure is objected to because it does not allow the public generally to determine quickly from a cursory inspection the nature and gist of the invention. Applicants should amend the abstract so that it corresponds to at least one independent claim. For example, Applicants should describe the limitations recited in claim 8 and the corresponding base claims. *See* 37 C.F.R. § 1.72. Should Applicants amend the claims in their next reply, the amended abstract should take into account any further limitations added to the broadest independent claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Cui *et al.*, *Science 293*:1289-1292 (**2001**).

Claim 1 is directed to a method of detecting a component of interest, comprising (a) providing one or more nanowires, which nanowires comprise one or more functional group, which functional group undergoes a change in charge in the presence of the component of interest; (b) contacting the one or more nanowires with a solution comprising the component of interest; which component produces the change in charge in the functional groups, which change in charge results in a detectable signal; and, detecting the signal, thereby detecting the component of interest.

Cui teaches the use of boron-doped silicon nanowires (SiNWs) to create highly sensitive, real-time electrically based sensors for biological and chemical species. Cui teaches that amine and oxide-functionalized SiNWs exhibit pH-dependent conductance that was linear over a large dynamic range and could be understood in terms of the change in surface charge during protonation and deprotonation. In reference to Figure 2, Cui states:

> "To explore biomolecular sensors, we functionalized SiNWs with biotin (20) and studied the well-characterized ligand-receptor binding of biotin-streptavidin (Fig. 2A) (21). Measurements show that the conductance of

> biotin-modified SiNWs increases rapidly to a constant value upon addition of a 250 nM streptavidin solution and that this conductance value is maintained after the addition of pure buffer solution (Fig. 2B). ***The increase in conductance upon addition of streptavidin is consistent with binding of a negatively charged species to the p-type SiNW surface and the fact that streptavidin (pI ~ 5 to 6) (21) is negatively charged at the pH of our measurements***. The absence of a conductance decrease with addition of pure buffer is also consistent with the small dissociation constant ($K_d \sim 10^{-15}$ M) and correspondingly small dissociation rate for biotinstreptavidin (21)."

Cui, page 1290, paragraph bridging columns 2 and 3 (emphasis added). Cui also teaches the detection of Ca^{2+} *via* immobilized calmodulin using the nanowire sensor (page 1291, column 3 through page 1292, column 1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 2 rejected under 35 U.S.C. § 103(a) as being unpatentable over Cui *et al.*, *Science 293*:1289-1292 (**2001**), in view of Bashir *et al.*, U.S. Patent No. 6,716,620, issued April 6, 2004.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1 is directed to a method of detecting a component of interest, comprising (a) providing one or more nanowires, which nanowires comprise one or more functional group,

which functional group undergoes a change in charge in the presence of the component of interest; (b) contacting the one or more nanowires with a solution comprising the component of interest; which component produces the change in charge in the functional groups, which change in charge results in a detectable signal; and, detecting the signal, thereby detecting the component of interest. Claim 2 requires the component of interest to be a nucleic acid.

Cui teaches the use of boron-doped silicon nanowires (SiNWs) to create highly sensitive, real-time electrically based sensors for biological and chemical species. Cui teaches that amine and oxide-functionalized SiNWs exhibit pH-dependent conductance that was linear over a large dynamic range and could be understood in terms of the change in surface charge during protonation and deprotonation. In reference to Figure 2, Cui states:

> "To explore biomolecular sensors, we functionalized SiNWs with biotin (20) and studied the well-characterized ligand-receptor binding of biotin-streptavidin (Fig. 2A) (21). Measurements show that the conductance of biotin-modified SiNWs increases rapidly to a constant value upon addition of a 250 nM streptavidin solution and that this conductance value is maintained after the addition of pure buffer solution (Fig. 2B). ***The increase in conductance upon addition of streptavidin is consistent with binding of a negatively charged species to the p-type SiNW surface and the fact that streptavidin (pI ~ 5 to 6) (21) is negatively charged at the pH of our measurements.*** The absence of a conductance decrease with addition of pure buffer is also consistent with the small dissociation constant ($K_d \sim 10^{-15}$ M) and correspondingly small dissociation rate for biotinstreptavidin (21)."

Cui, page 1290, paragraph bridging columns 2 and 3 (emphasis added). Cui also teaches the detection of Ca^{2+} *via* immobilized calmodulin using the nanowire sensor (page 1291, column 3 through page 1292, column 1).

Although Cui teaches that the component of interest may be calmodulin or biotin, Cui does not explicitly teach that the component of interest may be a DNA molecule/nucleic acid, as required by claim 2.

Bashir teaches a microscale biosensor for use in the detection of target biological substances including molecules and cells is a microfluidic system with integrated electronics, inlet-outlet ports and interface schemes, high sensitivity detection of pathogen specificity, and processing of biological materials at semiconductor interfaces. Bashir teaches that the capture

probes and analytes (*i.e.*, functional group and components of interest) may both be nucleic acids (col. 11, lines 48-56; and col. 12, lines 23-30). Bashir also teaches that detection occurs via a change in the charge at the FET:

> "The sensing of a target microbiological species such as a pathogenic bacterium in a detection chamber or cavity 34, 204, 206 may be implemented via circuit designs other than electrodes 36 (110, 112). For instance. A binding agent such as an avidin-biotinylated antibody may be attached to a gate of a silicon MOSFET. ***The MOSFET is a charge sensor where charge changes induced on the gate by the coupling of a target microbiological species become mirrored in a channel region under the gate insulator***. The device must be biased in the sub-threshold regime where the dI/dV_G slope is the maximum, i.e., the drain to the source current (I_{DS}) is maximum as a function of voltage on the gate (V_G). The device can be biased in the appropriate regime using the back bias or a dual gated MOSFET where the threshold of the top gate is controlled by the bottom gate. ***The double layer interfacial capacitance changes with the binding of the antigen and the related conformation changes***."

Bashir, col. 30, lines 50-67 (emphasis added).

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Cui and Bashir are directed to the development and use of semi-conductor based biosensor platforms that operate based on a change in charge. One of ordinary skill in the art would have been motivated by the use of the DNA detection format of Bashir for sequence specific verification of a given organism with the device of Cui that achieves low detection limits due to the nanowire detection format. Therefore, the invention as a whole was *prima facie* obvious at the time it was invented.

Claims 1 and 2 rejected under 35 U.S.C. § 103(a) as being unpatentable over Cui *et al.*, *Science 293*:1289-1292 (**2001**), in view of Lim *et al.*, U.S. Patent Appl. Pub. No. 2003/0102510 A1.

Claim 1 is directed to a method of detecting a component of interest, comprising (a) providing one or more nanowires, which nanowires comprise one or more functional group, which functional group undergoes a change in charge in the presence of the component of interest; (b) contacting the one or more nanowires with a solution comprising the component of interest; which component produces the change in charge in the functional groups, which change

in charge results in a detectable signal; and, detecting the signal, thereby detecting the component of interest. Claim 2 requires the component of interest to be a nucleic acid.

Cui teaches the use of boron-doped silicon nanowires (SiNWs) to create highly sensitive, real-time electrically based sensors for biological and chemical species. Cui teaches that amine and oxide-functionalized SiNWs exhibit pH-dependent conductance that was linear over a large dynamic range and could be understood in terms of the change in surface charge during protonation and deprotonation. In reference to Figure 2, Cui states:

> "To explore biomolecular sensors, we functionalized SiNWs with biotin (20) and studied the well-characterized ligand-receptor binding of biotin-streptavidin (Fig. 2A) (21). Measurements show that the conductance of biotin-modified SiNWs increases rapidly to a constant value upon addition of a 250 nM streptavidin solution and that this conductance value is maintained after the addition of pure buffer solution (Fig. 2B). ***The increase in conductance upon addition of streptavidin is consistent with binding of a negatively charged species to the p-type SiNW surface and the fact that streptavidin (pI ~ 5 to 6) (21) is negatively charged at the pH of our measurements***. The absence of a conductance decrease with addition of pure buffer is also consistent with the small dissociation constant ($K_d \sim 10^{-15}$ M) and correspondingly small dissociation rate for biotinstreptavidin (21)."

Cui, page 1290, paragraph bridging columns 2 and 3 (emphasis added). Cui also teaches the detection of Ca^{2+} *via* immobilized calmodulin using the nanowire sensor (page 1291, column 3 through page 1292, column 1).

Although Cui teaches that the component of interest may be calmodulin or biotin, Cui does not explicitly teach that the component of interest may be a DNA molecule/nucleic acid, as required by claim 2.

Lim teaches the use of a MOSFET based biosensor for the detection of nucleic acid hybridization assays:

> "In the present invention, a MOSFET is used as a sensor for detecting a charge variation before and after separation of double-stranded nucleic acid."

Lim, paragraph 0044. See also paragraph 0046.

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Cui and Lim are directed to the development

and use of semi-conductor based biosensor platforms that operate based on a change in charge. One of ordinary skill in the art would have been motivated by the use of the DNA detection format of Lim for sequence specific verification of a given organism with the device of Cui that achieves low detection limits due to the nanowire detection format. Therefore, the invention as a whole was *prima facie* obvious at the time it was invented.

Claims 1, 2 and 7, are rejected under 35 U.S.C. 103(a) as being unpatentable over Cui in view of Bashir and/or Lim, as applied to claims 1 and 2 above, and further in view of Zhao et al., 2001, *Nucleic Acids Research 29(4)*:955-959 (**2001**).

The limitations of claims 1 and 2, and the application of the prior art in the above rejections are hereby incorporated into the instant rejection.

Neither Cui, Bashir, or Lim teach that the component of interest be a hairpin oligonucleotide, as required by claim 7.

Zhao teaches a method for the immobilization of oligonucleotides useful in hybridization based assays, wherein the capture probes have hairpin structures with multiple surface attachment sites.

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Cui, Bashir, Lim and Zhao are directed to oligonucleotide-based hybridization assays. One of ordinary skill in the art would have recognized the advantages of the multipoint surface-attachment strategy with the hairpin oligonucleotide of Zhao, and its usefulness in any detection format, such as those taught by Cui, Bashir and/or Lim. Therefore, the invention as a whole was *prima facie* obvious at the time it was invented.

Claim 16 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Cui *et al.*, *Science 293*:1289-1292 (**2001**), in view of Brand *et al.*, *Appl Microbiol Biotechnol 36(2)*:167-72 (**1991**).

Claim 16 is directed to a method of providing one or more nanowires with immobilized glucose oxidase for glucose detection based on a pH change at the nanowire surface.

Cui teaches the use of boron-doped silicon nanowires (SiNWs) to create highly sensitive, real-time electrically based sensors for biological and chemical species. Cui teaches that amine and oxide-functionalized SiNWs exhibit pH-dependent conductance that was linear over a large dynamic range and could be understood in terms of the change in surface charge during protonation and deprotonation. In reference to Figure 2, Cui states:

> "To explore biomolecular sensors, we functionalized SiNWs with biotin (20) and studied the well-characterized ligand-receptor binding of biotin-streptavidin (Fig. 2A) (21). Measurements show that the conductance of biotin-modified SiNWs increases rapidly to a constant value upon addition of a 250 nM streptavidin solution and that this conductance value is maintained after the addition of pure buffer solution (Fig. 2B). ***The increase in conductance upon addition of streptavidin is consistent with binding of a negatively charged species to the p-type SiNW surface and the fact that streptavidin (pI ~ 5 to 6) (21) is negatively charged at the pH of our measurements***. The absence of a conductance decrease with addition of pure buffer is also consistent with the small dissociation constant ($K_d \sim 10^{-15}$ M) and correspondingly small dissociation rate for biotinstreptavidin (21)."

Cui, page 1290, paragraph bridging columns 2 and 3 (emphasis added). Cui also teaches the detection of Ca^{2+} *via* immobilized calmodulin using the nanowire sensor (page 1291, column 3 through page 1292, column 1).

Although Cui teaches that the component of interest may be Ca^{2+}/calmodulin or antibodies/biotin, Cui does not explicitly teach that the component of interest may be glucose detected by a pH change created by a reaction with immobilized glucose oxidase.

Brand discloses single and multisensor field effect transistors (FET) with a pH-sensitive Si/SiO2/Si3N4/Ta2O5-gate and reference electrode (for single sensor) with glucose oxidase-FET (GOD-FET) were developed and used for glucose analysis.

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Cui and Brand are directed to the development and use of semi-conductor based biosensor platforms that operate based on a change in charge. One of ordinary skill in the art would have been recognized the advantages of the glucose oxidase-FET sensor for glucose detection that is sensitive to pH/charge perturbations as taught by Brand to be combined with the nanowire device of Cui that achieves low detection

limits due to the nanowire detection format. Therefore, the invention as a whole was *prima facie* obvious at the time it was invented.

Objection to Dependent Claims

Claims 8 and 9 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusions

No claim is allowable.

If Applicants should amendment the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipsis verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSL

JON EPPERSON, PH.D.
PATENT EXAMINER